

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claim 1 (currently amended): A ~~non-human~~ transgenic mouse animal whose genome comprises a nucleotide sequence encoding human CD20.

Claim 2 (currently amended): The transgenic mouse animal of claim 1 wherein said nucleotide sequence is operably linked to a human endogenous promoter.

Claim 3 (currently amended): The transgenic mouse animal of claim 2 whose cells express human CD20.

Claim 4 (currently amended): The transgenic mouse animal of claim 3 wherein human CD20 is expressed on the surface of B lymphocytes.

Claim 5 (currently amended): The transgenic mouse animal of claim 3 wherein human CD20 is expressed on the B lymphocytes at a level sufficient for anti-human CD20 antibody bound to the expressing cells to affect killing of the cells, resulting in B cell depletion.

Claim 6 (currently amended): The transgenic mouse animal of claim 1 wherein the genome of said mouse animal contains a disruption in an endogenous gene encoding a CD20 molecule substantially homologous to human CD20.

Claim 7 (currently amended): The transgenic mouse animal of claim 6, wherein the endogenous gene encodes a murine CD20.

Claim 8 (currently amended): A method of identifying an agent capable of treating a B cell lymphoma said method comprising: a) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse animal of claim 1; b) administering said agent to the mouse animal of claim 1; and c) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse animal; wherein a decrease in the number of B lymphocytes

and/or pre-B cells expressing human CD20 in the mouse animal after treatment with the agent identifies the agent capable of treating a B cell lymphoma.

Claim 9 (canceled)

Claim 10 (currently amended): A method of identifying an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing human CD20 said method comprising: a) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse an animal of claim 1; b) administering said agent to the mouse animal of claim 1; and c) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse animal; wherein a decrease in the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse animal identifies the agent as capable of depleting or killing B lymphocytes and/or pre-B cells expressing CD20.

Claim 11 (original): The method of claim 10 wherein said cells are cancer cells.

Claim 12 (canceled)

Claim 13 (currently amended): A cell or tissue derived from the transgenic mouse animal of claim 1.

Claim 14 (canceled)

Claim 15 (canceled)

Claim 16 (currently amended): A method of testing safety of anti-human CD20 therapy, said method comprising: a) ~~measuring the level of B lymphocytes expressing human CD20 in an animal of claim 1;~~ b) ~~administering said agent to the animal of claim 1;~~ and c) ~~measuring the level of B lymphocytes expressing human CD20 in the animal;~~ wherein a decrease in the number of B lymphocytes expressing human CD20 in the animal identifies the agent as capable of depleting or killing cells expressing CD20; d) monitoring monitoring a mouse of claim 1 that has been administered an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing CD20the animal for short or long term adverse effects.

Claim 17 (currently amended): A method of testing efficacy of anti-human CD20 therapy, said method comprising: ~~a) measuring the level of B lymphocytes expressing human CD20 in a set of animals of claim 1; b) administering to each animal of the set a different dose of an agent; and c) measuring the level of B lymphocytes expressing human CD20 in animal after each dose; and d) determining at least one dose of an agent that results in the most B cell depletion in a set of mice of claim 1 that have each been administered a different dose of the agent; wherein the amount of B cell depletion is determined by measuring the number of B lymphocytes and/or pre-B cells expressing human CD20 in the set of mice of claim 1.~~

Claim 18 (new): The transgenic mouse of claim 2 wherein the promoter is a human CD20 promoter.

Claim 19 (new): The transgenic mouse of claim 1 wherein said nucleotide sequence is operably linked to a murine CD20 promoter.

Claim 20 (new): The method of claim 8 wherein the number of B lymphocytes is measured.

Claim 21 (new): The method of claim 10 wherein the number of B lymphocytes is measured.

Claim 22 (new): The method of claim 16 wherein the agent decreases the number of B lymphocytes.

Claim 23 (new): The method of claim 17 wherein the number of B lymphocytes is measured.

Claim 24 (new): A method of identifying an agent capable of treating a B cell lymphoma said method comprising comparing the number of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse of claim 1 after administering an agent to the mouse to the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse before administration of the agent, wherein a decrease in the number of B lymphocytes and/or pre-B cells expression human CD20 in the mouse after administration of the agent compared to the number of B lymphocytes

and/or pre-B cells expressing human CD20 in the mouse before administration of the agent identifies the agent capable of treating a B cell lymphoma.

Claim 25 (new): The method of claim 24 wherein the number of B lymphocytes is measured.

Claim 26 (new): A method of identifying an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing human CD20 said method comprising comparing the number of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse of claim 1 after administering an agent to the mouse to the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse before administration of the agent, wherein a decrease in the number of B lymphocytes and/or pre-B cells expression human CD20 in the mouse after administration of the agent compared to the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse before administration of the agent identifies the agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing CD20.

Claim 27 (new): The method of claim 26 wherein said cells are cancer cells.

Claim 28 (new): The method of claim 26 wherein the number of B lymphocytes is measured.